National Vital Statistics Reports



Volume 68, Number 3 March 21, 2019

Drug Overdose Deaths Involving Fentanyl, 2011–2016

by Merianne Rose Spencer, M.P.H., Margaret Warner, Ph.D., and Brigham A. Bastian, B.S., National Center for Health Statistics; James P. Trinidad, M.P.H., M.S., U.S. Food and Drug Administration; and Holly Hedegaard, M.D., M.S.P.H., National Center for Health Statistics

Abstract

Objectives—Fentanyl, a synthetic opioid, has been increasingly identified in drug overdose deaths. This report describes trends in drug overdose deaths involving fentanyl by demographic characteristics and geographic regions from 2011 through 2016.

Methods-Drug overdose deaths were identified from the National Vital Statistics System-Mortality (NVSS-M) multiple cause-of-death files (2011-2016) using International Classification of Diseases, 10th Revision underlying causes of death (codes X40-X44, X60-X64, X85, or Y10-Y14). NVSS-M records for drug overdose deaths were linked with literal text from death certificates. Drug overdose deaths involving fentanyl were identified using a methodology established collaboratively by the National Center for Health Statistics and U.S. Food and Drug Administration—referred to as the Drugs Mentioned with Involvement (DMI) methodology—supplemented with search terms identified using text analytics software. Fentanyl involvement was determined by the presence of any string term or phrase listing fentanyl, or any fentanyl metabolite, precursor, analog, or misspelling identified in the death certificate literal text fields (i.e., the causes of death from Part I, significant conditions contributing to death from Part II, and a description of how the injury occurred). Trends were evaluated using the National Cancer Institute's Joinpoint Regression Program.

Results—The number of drug overdose deaths involving fentanyl was stable in 2011 (1,663) and 2012 (1,615), and began to increase in 2013, rising to 18,335 deaths in 2016. The age-adjusted rate increased from 0.5 per 100,000 standard population in 2011 to 5.9 per 100,000 in 2016, with the increase starting in 2013 (0.6 in 2013 to 1.3 in 2014 and 2.6 in 2015). Numbers and rates increased for all sex, age, and racial and ethnic subgroups, and most public health regions. Adjustment for improved drug

reporting over the study period did not change the trend patterns observed.

Conclusions—This report illustrates the rise in drug overdose deaths involving fentanyl from 2011 through 2016 nationally, and by age, sex, race and ethnicity, and public health region. Understanding national trends and patterns for drug overdose deaths involving fentanyl may inform public health policies and practices.

Keywords: National Vital Statistics System • national trends • mortality • death certificate literal text

Introduction

Fentanyl is a synthetic opioid that has been involved increasingly in drug overdose deaths (1–11). In 2011 and 2012, fentanyl was involved in roughly 1,600 drug overdose deaths each year, but from 2012 through 2014, the number of drug overdose deaths involving fentanyl more than doubled each year (1). State-based analyses suggest that the recent increase in overdose deaths involving fentanyl may be related to increased availability of illicitly manufactured fentanyl (3,4,9–11). Illicitly manufactured fentanyl includes various analogs (e.g., acetylfentanyl, carfentanil, furanyl fentanyl) that vary in potency and can be lethal in very low concentrations (3).

National mortality statistics on drug overdose deaths have traditionally used the *International Classification of Diseases*, 10th Revision (ICD-10) to classify and monitor drugs involved in deaths (12). However, ICD-10 is limited to broader categories (e.g., synthetic opioids other than methadone) that make it difficult to identify deaths involving specific drugs of interest (e.g., fentanyl or illicitly manufactured fentanyl analogs). The National Center for Health Statistics (NCHS) and the U.S. Food and Drug Administration (FDA) collaboratively developed methods, referred to as the Drugs Mentioned with Involvement (DMI) methodology, to analyze literal text data from death





certificates to identify specific drugs involved in deaths (13). A recent study using the DMI methodology found that fentanyl was the ninth most frequently mentioned drug involved in overdose deaths in 2013 and the most frequently mentioned drug in 2016 (2). It also showed that deaths involving fentanyl often involved other drugs. For example, in 2016, nearly 70% of deaths involving fentanyl also involved one or more other drugs, such as heroin or cocaine (2).

This report describes the trends in drug overdose deaths involving fentanyl from 2011 through 2016, using mortality data from the National Vital Statistics System linked to literal text information from death certificates. Temporal trends, geographic patterns, and differences among demographic groups are presented.

Methods

Data sources

This descriptive study analyzed National Vital Statistics System mortality (NVSS-M) multiple cause-of-death data from 2011 through 2016. NVSS-M contains information extracted from death certificates on cause of death and demographic and geographic factors (14). The study population was limited to U.S. residents. Drug overdose deaths were identified using ICD-10 underlying cause-of-death codes X40-X44, X60-X64, X85, and Y10-Y14. These underlying-cause codes identify the deaths due to acute toxicity from drugs (i.e., drug overdose) rather than to chronic exposure leading to death (e.g., liver toxicity) or adverse effects from therapeutic or prophylactic dosages of drugs. Drug overdose deaths include all intents (i.e., unintentional, suicide, homicide, and undetermined intent). Use of these underlying cause-of-death codes is consistent with other NCHS publications on drug overdose deaths and facilitates comparisons with other analyses using ICD-10-coded data (1,2,15).

NVSS-M records for drug overdose deaths were linked to literal text data from death certificates. The literal text is the written information provided by the medical certifier, usually a medical examiner or coroner in the case of drug overdose deaths, that describes the cause of death as well as other factors or circumstances that contributed to the death (16,17). Literal text from three fields of the death certificate—the causes of death from Part I, the other significant conditions contributing to death from Part II, and the description of how the injury occurred—was analyzed to identify the specific drugs involved in the overdose death.

Identifying drug overdose deaths involving fentanyl

This report used the DMI methodology (13) informed by the results from an exploratory analysis of the literal text using SAS Contextual Analysis software (18). The DMI methodology (13) searches the literal text fields of NVSS-M data for mentions of drugs and for terms that provide context about involvement of the drug in the death (i.e., whether the drug contributed to the death). Drugs mentioned in the death certificate literal text

are assumed to be involved in the death unless contextual information suggests otherwise (13). For example, "METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS INFECTION" does not suggest drug involvement in mortality, but rather a type of bacterial infection. Similarly, the phrase "NOT DRUG RELATED" clearly indicates that drugs were not involved in the death even though "DRUG" is included in the phrase.

To supplement the DMI methodology, SAS Contextual Analysis software (18) was used to identify additional search terms. Linguistic rules were defined to search for new drug misspellings; precursors; metabolites; analogs of fentanyl, including those containing special characters, numbers, and dashes; and to identify forms that may be illicit (e.g., acetylfentanyl, carfentanil) or are brand or prescription forms of fentanyl (e.g., duragesic, sufentanil, remifentanil). The additional search terms identified using the contextual software were incorporated into the DMI methodology and are described in the Technical Notes. With the expanded list of search terms, the total number of drug overdose deaths identified as involving fentanyl was slightly higher than previously reported (7 deaths in 2011, 10 deaths in 2012, 14 deaths in 2013, and 23 deaths in 2014) (1).

Analysis

For this report, the label "drug overdose deaths involving fentanyl" includes drug overdose deaths involving fentanyl, whether prescription or illicitly manufactured, as well as deaths involving any fentanyl metabolites, precursors, or analogs as identified in the death certificate literal text (see Technical Notes). The numbers and rates for drug overdoses involving fentanyl were calculated and compared by demographic and geographic region. Bridged-race vintage postcensal resident population estimates were used to calculate death rates (14). Age-adjusted death rates were calculated using the direct method and the 2000 standard U.S. population (14). Unless otherwise noted, rates in the text refer to age-adjusted rates.

Geographic patterns in overdose deaths involving fentanyl are presented by the U.S. Department of Health and Human Services (HHS) 10 public health regions. These regions are used for public health prevention, preparedness, and agency-wide coordination of HHS programs and policies (19). These regions, excluding U.S. territories, are:

- Region 1—Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont
- Region 2—New Jersey, New York, New York City
- Region 3—Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, West Virginia
- Region 4—Alabama, Florida, Georgia, Kentucky, Mississippi, South Carolina, Tennessee
- Region 5—Illinois, Indiana, Michigan, Minnesota, Ohio, Wisconsin
- Region 6—Arkansas, Louisiana, New Mexico, Oklahoma, Texas
- Region 7—Iowa, Kansas, Missouri, Nebraska

- Region 8—Colorado, Montana, North Dakota, South Dakota, Utah, Wyoming
- Region 9—Arizona, California, Hawaii, Nevada
- Region 10—Alaska, Idaho, Oregon, Washington

Trends in rates for drug overdose deaths involving fentanyl were evaluated using the National Cancer Institute's Joinpoint Regression Program Version 4.6.0.0 (20). Joinpoint software fitted weighted least-squares regression models to the rates on the log transform scale. Allowing one observed time point at each end and two for the middle line segments, the Grid Search Algorithm searched for a maximum of two joinpoints at an overall alpha level of p < 0.05 (21). Pairwise comparisons of trend segments among subgroups were also analyzed, with Bonferonni adjustment (20). Rates between subgroups were compared using a z test at the 0.05 level of significance (14). Unless otherwise stated, any mention of an increase in rates indicates a statistically significant change.

Assessment for improved reporting on death certificates

The ICD-10 multiple-cause codes T36-T50.8 provide information on the types of drugs or drug classes involved in the death. The ICD-10 multiple-cause code T50.9 indicates a nonspecific reference to a drug (e.g., "multidrug," "polypharmacy," "drug"). The percentage of deaths with an underlying cause of X40-X44, X60-X64, X85, or Y10-Y14 that had a multiple-cause code of T36-T50.8 is a measure of the specificity of reporting drugs or drug classes in drug overdose deaths. This measure was used to assess possible changes in reporting of specific drugs and drug classes through the years of the study. The percentage of drug overdose deaths coded with T36-T50.8 increased each year (75.0% in 2011, 76.0% in 2012, 77.9% in 2013, 80.7% in 2014, 83.1% in 2015, and 85.4% in 2016) (21,22).

To assess the possible impact of lower reporting of specific drugs in the years prior to 2016, an adjustment factor accounting for improved reporting of specific drugs over the time period was applied to each age-adjusted rate for drug overdose deaths involving fentanyl (i.e., by year, sex, age, race and ethnicity, and public health region). The adjustment factor assumed that the specificity of drug reporting had remained constant from 2011 through 2016 at the 2016 drug specificity rate; the adjustment factor was recalculated and applied to each age-adjusted rate for the stratified analyses (i.e., demographic and geographic groups). Results from this analysis show similar trends for both the observed and adjusted values (see Technical Notes). The following results reflect the numbers and rates based on observed values. The number of drug overdose deaths involving any particular drug in any particular year should be considered the minimum number, as there may be additional deaths in which the drug was involved but not specified on the death certificate literal text. All results should be interpreted in light of the improved reporting of specific drugs in the literal text over time.

Results

Number and percentage of drug overdose deaths involving fentanyl

Annually, the number of drug overdose deaths involving fentanyl was stable in 2011 (1,663) and 2012 (1,615), and began to increase in 2013 (1,919), rising to 18,335 deaths in 2016 (Table 1). From 2013 through 2016, the number of deaths approximately doubled each year. From 2011 through the third quarter of 2013, there were fewer than 500 fentanyl-involved deaths per quarter (Figure 1, Table 1). Beginning in the last quarter of 2013 through 2016, the number of deaths involving fentanyl increased nearly every quarter to more than 5,800 deaths.

Crude and age-adjusted rates of drug overdose deaths involving fentanyl

The age-adjusted rate of drug overdose deaths involving fentanyl was 0.5 per 100,000 in 2011 and 2012, and approximately doubled each year from 0.6 (2013) to 1.3 (2014) to 2.6 (2015) to 5.9 (2016) (Figure 2, Table 2). From 2011 through 2013, there was no statistical change in the age-adjusted rates, but from 2013 through 2016, the rates increased on average by about 113% per year. The crude rates were similar to the age-adjusted rates for the study period.

Rates of drug overdose deaths involving fentanyl by sex of decedent

For males, age-adjusted rates for drug overdose deaths were stable from 2011 through 2013, and then increased by 125.6% per year from 2013 through 2016 (Figure 3, Tables 2 and 3). For females, the age-adjusted rates increased exponentially from 2011 through 2016. In 2011, 2012, and 2013, the rates for males and females were similar at 0.6 to 0.7 per 100,000 for males, and 0.4 to 0.5 for females. Starting in 2013, the rates diverged, with the rate for males increasing more rapidly than the rate for females. By 2016, the rate for males (8.6) was 2.8 times the rate for females (3.1).

Rates of drug overdose deaths involving fentanyl by age group

Exponential increases in rates from 2011 through 2016 were observed among all age groups (Figure 4, Tables 2 and 3). The largest average annual percent change from 2011 through 2016 occurred among young adults aged 25–34 (100.0% per year) and 15–24 (93.9% per year). The smallest average annual percent change occurred among adults aged 65 and over (41.6% per year). The rate for adults aged 35–44 was stable from 2011 through 2013, then increased by 123.7% per year from 2013 through 2016. In 2016, the rates were highest among adults aged 25–34 and 35–44 at 13.4 and 11.4 per 100,000, respectively.

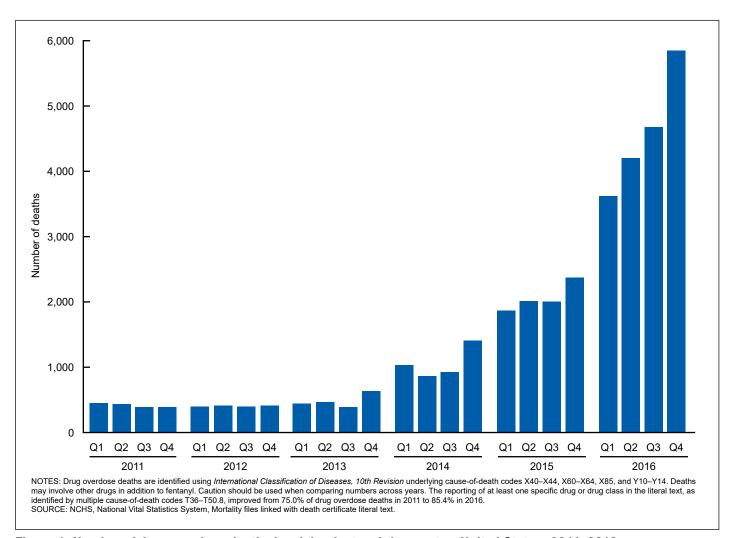


Figure 1. Number of drug overdose deaths involving fentanyl, by quarter: United States, 2011-2016

Rates of drug overdose deaths involving fentanyl by race and ethnicity

The age-adjusted rates for drug overdose deaths involving fentanyl increased exponentially among all the racial and ethnic subgroups examined (Figure 5, Tables 2 and 3). Rates for non-Hispanic white persons ranged from 0.7 to 0.8 per 100,000 from 2011 through 2013, then increased by 108.8% from 2013 through 2016. Non-Hispanic black persons had the largest annual percentage increase in rates from 2011 through 2016 (140.6% per year), followed by Hispanic persons (118.3% per year). Rates for non-Hispanic white persons were greater than other subgroups throughout the study period. The rates for non-Hispanic black and Hispanic persons were similar from 2011 through 2013, then diverged from 2014 through 2016. In 2016, the rates were highest among non-Hispanic white persons (7.7), followed by non-Hispanic black (5.6) and Hispanic (2.5) persons.

Rates of drug overdose deaths involving fentanyl by public health region

Rates of drug overdose deaths involving fentanyl increased exponentially from 2011 through 2016 for most public health regions (Figure 6, Tables 2 and 3). The greatest rate increases were in Region 1 (CT, ME, MA, NH, RI, and VT), Region 2 (NJ, NY, and NYC), Region 3 (DE, DC, MD, PA, VA, and WV), and Region 5 (IL, IN, MI, MN, OH, and WI), which increased 113.9%, 10.9%, 103.6%, and 102.2% per year, respectively. Rates were similar across all public health regions in 2011. In 2016, the rates for Regions 1, 2, 3, 4, and 5 were higher than for Regions 6, 8, 9, and 10. In 2016, rates ranged from 0.8 per 100,000 (Region 9) to 19.8 (Region 1).

Discussion

This report illustrates the rise in drug overdose deaths involving fentanyl in the United States from 2011 through 2016. The number of drug overdose deaths involving fentanyl increased from 1,663 in 2011 to 18,335 in 2016. Beginning in the fourth quarter of 2013, the number of deaths increased every quarter. From 2013 through 2014, the death rate more than doubled,

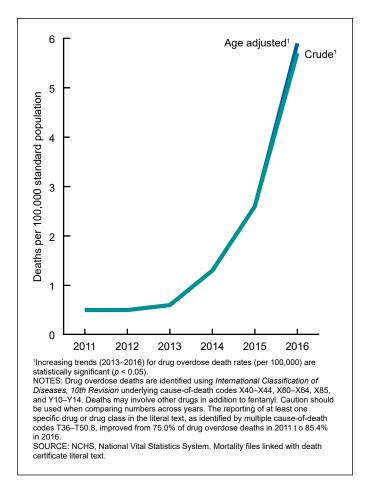


Figure 2. Crude and age-adjusted rates for drug overdose deaths involving fentanyl, by year: United States, 2011–2016

nearly doubled again from 2014 through 2015, and more than doubled again from 2015 through 2016.

The rate of drug overdose deaths involving fentanyl increased exponentially for both sexes, with the rate increasing more rapidly for males than for females. Rates also increased exponentially across all age groups, with the greatest increases among those aged 15–24 and 25–34. Exponential increases were also seen for rates among race and ethnicity groups. Non-Hispanic black persons had the largest annual percentage increase in rates, followed by Hispanic persons, while in 2016, the rate was highest for non-Hispanic white persons. Rates increased exponentially for most public health regions, however, the increase was greatest in Regions 1, 2, 3, and 5 (i.e., East Coast and Upper Midwest).

Limitations

Monitoring national trends in drug overdose deaths depends on the quality and completeness of information provided on death certificates. Variation in death investigation, autopsy, and toxicology practices across medicolegal death investigation jurisdictions contributes to inconsistencies in how the manner and cause of death are reported (23,24). For example, differences in toxicological testing practices, such as when and how the

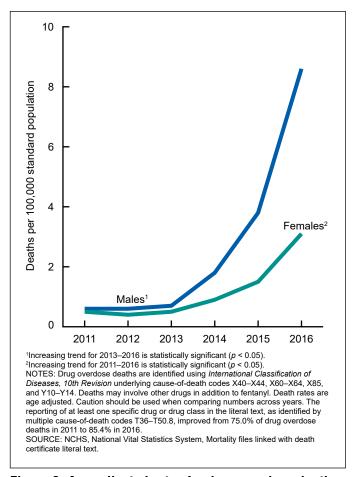


Figure 3. Age-adjusted rates for drug overdose deaths involving fentanyl, by sex of the decedent: United States, 2011–2016

testing is performed, which substances are tested for, and the interpretation of the test results, can impact whether fentanyl is detected and reported on the death certificate. Because of these limitations, the number of drug overdose deaths involving any particular drug in any particular year should be considered the minimum number, as there may be additional deaths in which the drug was involved but not specified on the death certificate literal text.

Variations in the way drug overdose deaths are reported on the death certificates, including the level of detail on the specific drugs involved, impacts comparability. Trends in rates should be interpreted in light of the improvements in the quality of the data during the study period. For example, some of the observed increases in the rates are likely attributable to improvements in reporting. During the study period, the reporting of at least one specific drug in the literal text improved from 75% of drug overdose deaths in 2011 to 85% of drug overdose deaths in 2016 (2,22). To account for improved reporting of specific drugs over the time period, an adjustment factor, which took into account what the drug overdose death rate involving fentanyl would have been had the drug specificity been uniform from 2011 through 2016, was applied to the rates. The adjustments for improved reporting did not change the patterns observed.

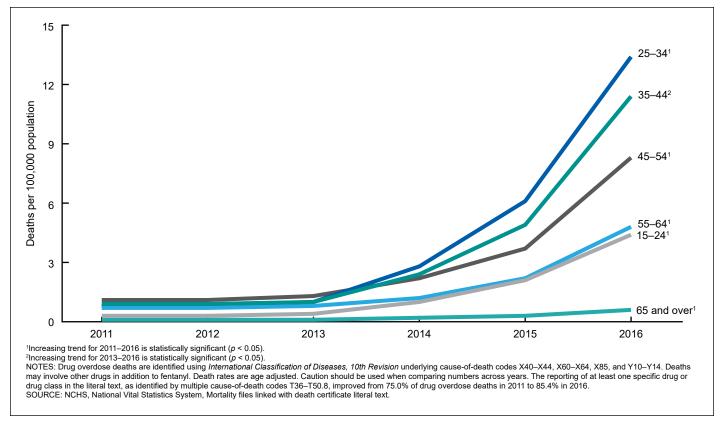


Figure 4. Rates for drug overdose deaths involving fentanyl, by age group: United States, 2011–2016

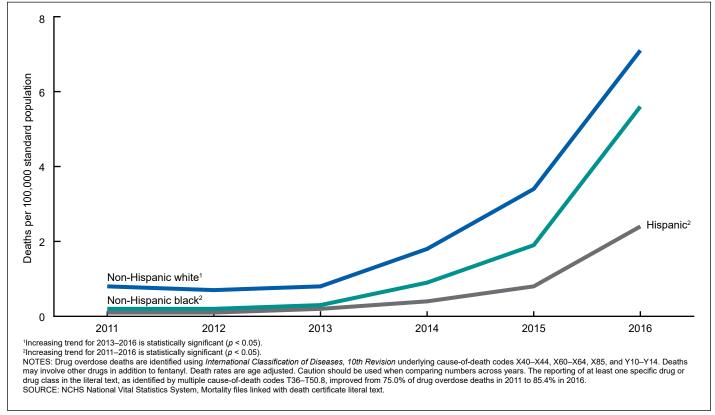


Figure 5. Age-adjusted rates for drug overdose deaths involving fentanyl, by race and ethnicity: United States, 2011–2016

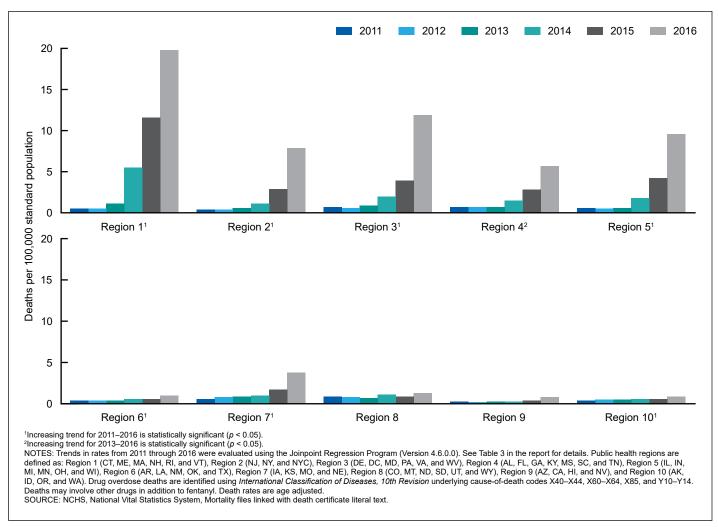


Figure 6. Age-adjusted rates for drug overdose deaths involving fentanyl, by public health region: United States, 2011–2016

The absence of drug-specific information on the death certificate does not mean that fentanyl was not present; rather, it may suggest that toxicology tests were not performed or were inadequate to detect the drug. Also, new fentanyl analogs are being identified with increasing frequency and are often lethal in very low concentrations. Detection of these substances requires new testing materials and continuous recalibration of toxicology laboratory equipment (16), both of which can be complicated and expensive, thus further contributing to variation in death reporting across the country.

The need to understand the factors influencing overdoses and deaths involving fentanyl has resulted in collaboration among public health agencies, medical examiners and coroners, and public safety agencies. These collaborations will contribute to better detection and reporting on death certificates, which in turn, will help improve quality of local, state, and national vital statistics data.

Conclusion

Fentanyl is increasingly involved in drug overdose deaths nationally. This report uses NVSS-M data, enhanced with literal text from death certificates, to provide a picture of temporal trends, demographic characteristics, and geographic patterns of fentanyl-involved drug overdose deaths in the United States from 2011 through 2016.

References

- Warner M, Trinidad JP, Bastian BA, Miniño AM, Hedegaard H. Drugs most frequently involved in drug overdose deaths: United States, 2010–2014. National Vital Statistics Reports; vol 65 no 10. Hyattsville, MD: National Center for Health Statistics. 2016.
- Hedegaard H, Bastian BA, Trinidad JP, Spencer M, Warner M. Drugs most frequently involved in drug overdose deaths: United States, 2011–2016. National Vital Statistics Reports; vol 67 no 9. Hyattsville, MD: National Center for Health Statistics. 2018.
- 3. Peterson AB, Gladden RM, Delcher C, Spies E, Garcia-Williams A, Wang Y, et al. Increases in fentanyl-related overdose deaths—Florida and Ohio, 2013–2015. MMWR Morb Mortal Wkly Rep 65(33):844–9. 2016.

- 8
- Gladden RM, Martinez P, Seth P. Fentanyl law enforcement submissions and increases in synthetic opioid-involved overdose deaths—27 states, 2013–2014. MMWR Morb Mortal Wkly Rep 65(33):837–43. 2016.
- Frank RG, Pollack HA. Addressing the fentanyl threat to public health. N Engl J Med 376(7):605–7. 2017.
- Centers for Disease Control and Prevention. CDC Health Alert Network (HAN) update: Rising numbers of deaths involving fentanyl and fentanyl analogs, including carfentanil, and increased usage and mixing of non-opioids [press release]. July 11, 2018. Available from: https://content.govdelivery.com/accounts/USCDC/ bulletins/1fdd63b.
- Jones CM, Einstein EB, Compton WM. Changes in synthetic opioid involvement in drug overdose deaths in the United States, 2010–2016. JAMA 319(17):1819–21. 2018.
- Rudd RA, Seth P, David F, Scholl L. Increases in drug and opioidinvolved overdose deaths—United States, 2010–2015. MMWR Morb Mortal Wkly Rep 65(50–51):1445–52. 2016.
- O'Donnell JK, Halpin J, Mattson CL, Goldberger BA, Gladden RM. Deaths involving fentanyl, fentanyl analogs, and U-47700—10 states, July-December 2016. MMWR Morb Mortal Wkly Rep 66(43):1197-1202. 2017.
- Somerville NJ, O'Donnell J, Gladden RM, Zibbell JE, Green TC, Younkin M, et al. Characteristics of fentanyl overdose— Massachusetts, 2014–2016. MMWR Morb Mortal Wkly Rep 66(14):382–6. 2017.
- 11. Suzuki J, El-Haddad S. A review: Fentanyl and non-pharmaceutical fentanyls. Drug and Alcohol Depend 171:107–16. 2017.
- World Health Organization. International statistical classification of diseases and related health problems, 10th revision (ICD-10). 2nd ed. Geneva, Switzerland. 2004.
- Trinidad JP, Warner M, Bastian BA, Miniño AM, Hedegaard H. Using literal text from the death certificate to enhance mortality statistics: Characterizing drug involvement in deaths. National Vital Statistics Reports; vol 65 no 9. Hyattsville, MD: National Center for Health Statistics. 2016.
- 14. Xu JQ, Murphy SL, Kochanek KD, Bastian B, Arias E. Deaths: Final data for 2016. National Vital Statistics Reports; vol 67 no 5. Hyattsville, MD: National Center for Health Statistics. 2018.
- Hedegaard H, Warner M, Miniño AM. Drug overdose deaths in the United States, 1999–2016. NCHS Data Brief, no 294. Hyattsville, MD: National Center for Health Statistics. 2017.
- 16. Davis GG. National Association of Medical Examiners position paper: Recommendations for the investigation, diagnosis, and certification of deaths related to opioid drugs. J Med Toxicol 10(1):100–6. 2014.
- 17. National Center for Health Statistics. Medical examiners' and coroners' handbook on death registration and fetal death reporting. 2003.
- 18. SAS Institute, Inc. SAS contextual analysis (Release 14.1 edition) [computer software]. 2016.
- U.S. Department of Health and Human Services. Regional offices. Available from: https://www.hhs.gov/about/agencies/regional-offices/index.html.
- 20. National Cancer Institute. Joinpoint Regression Program (Version 3.4.3) [computer software]. 2010.
- Ingram DD, Malec DJ, Makuc DM, Kruszon-Moran D, Gindi RM, Albert M, et al. National Center for Health Statistics Guidelines for Analysis of Trends. National Center for Health Statistics. Vital Health Stat 2(179). 2018. Available from: https://www.cdc.gov/nchs/data/series/sr_02/sr02_179.pdf.
- Centers for Disease Control and Prevention, National Center for Health Statistics. About multiple cause of death, 1999–2017. CDC

- WONDER Online Database, released December 2017. Data from the Multiple Cause of Death Files, 1999–2016, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Available from: https://wonder.cdc.gov/mcd-icd10.html.
- 23. Warner M, Paulozzi LJ, Nolte KB, Davis GG, Nelson LS. State variation in certifying manner of death and drugs involved in drug intoxication deaths. AFP Journal 3(2):231–7. 2013.
- 24. Hanzlick RL. A perspective on medicolegal death investigation in the United States: 2013. Acad Forensic Pathol 4(1):2–9. 2014.
- 25. United States Drug Enforcement Administration. Scientific Working Group for the Analysis of Seized Drugs. Available from: http://swgdrug.org/monographs.htm.
- 26. U.S. Food and Drug Administration, National Library of Medicine. Substance Registration System—Unique ingredient identifier. Available from: https://fdasis.nlm.nih.gov/srs.

List of Detailed Tables

1.	Number of drug overdose deaths involving fentanyl and percent of the annual total, by year and guarter: United States, 2011–	
	2016	9
2.	Numbers and crude and age-adjusted rates for drug overdose deaths involving fentanyl, by sex, age, race and Hispanic origin, and public health region: United States,	
	2011–2016	10
3.	Trends in age-adjusted rates for drug overdose deaths involving fentanyl, by sex, age, race and Hispanic origin, and public health	
	region: United States, 2011–2016	12

Table 1. Number of drug overdose deaths involving fentanyl and percent of the annual total, by year and quarter: United States, 2011–2016

Year and quarter	Number	Percent
2011	1,663	100.0
Quarter 1	449	27.0
Quarter 2	432	26.0
Quarter 3	391	23.5
Quarter 4	391	23.5
2012	1,615	100.0
Quarter 1	398	24.6
Quarter 2	412	25.5
Quarter 3	397	24.6
Quarter 4	408	25.3
2013	1,919	100.0
Quarter 1	438	22.8
Quarter 2	461	24.0
Quarter 3	385	20.1
Quarter 4	635	33.1
2014	4,223	100.0
Quarter 1	1,031	24.4
Quarter 2	861	20.4
Quarter 3	925	21.9
Quarter 4	1,406	33.3
2015	8,251	100.0
Quarter 1	1,863	22.6
Quarter 2	2,009	24.3
Quarter 3	2,005	24.3
Quarter 4	2,374	28.8
2016	18,335	100.0
Quarter 1	3,617	19.7
Quarter 2	4,197	22.9
Quarter 3	4,673	25.5
Quarter 4	5,848	31.9

NOTES: Drug overdose deaths are identified using *International Classification of Diseases*, 10th Revision underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to fentanyl. Caution should be used when comparing numbers across years. The reporting of at least one specific drug or drug class in the literal text, as identified by multiple cause-of-death codes T36–T50.8, improved from 75.0% of drug overdose deaths in 2011 to 85.4% in 2016.

Table 2. Numbers and crude and age-adjusted rates for drug overdose deaths involving fentanyl, by sex, age, race and Hispanic origin, and public health region: United States, 2011–2016

Characteristic	2011	2012	2013	2014	2015	2016
			Number			
II drug overdose deaths	1,663	1,615	1,919	4,223	8,251	18,335
Sex						
/lale	916	912	1,107	2,827	5,945	13,413
emale	747	703	812	1,396	2,306	4,922
Age group (years)						
5–24	129	110	160	453	927	1,924
5–34	325	332	415	1,223	2,691	5,976
5–44	378	350	399	992	1,990	4,615
5–54	505	498	552	971	1,605	3,531
						1,980
5–64	264	261	325	489	897	1,980
5 and over	55	61	66	91	135	299
Race and Hispanic origin						
Ion-Hispanic white	1,507	1,462	1,684	3,569	6,855	14,236
on-Hispanic black	63	62	111	358	800	2,357
ispanic	60	50	95	223	447	1,399
Public health region ¹						
(CT, ME, MA, NH, RI, VT)	80	77	160	775	1,621	2,745
(NJ, NY, NYC)	114	115	180	328	830	2,241
· · · · /						
(DE, DC, MD, PA, VA, WV)	209	191	283	596	1,163	3,545
(AL, FL, GA, KY, MS, SC, TN)	406	405	433	906	1,694	3,460
(IL, IN, MI, MN, OH, WI)	299	274	290	910	2,074	4,790
(AR, LA, NM, OK, TX)	147	166	167	224	257	393
(IA, KS, MO, NE)	85	103	120	133	221	489
(CO, MT, ND, SD, UT, WY)	103	88	80	117	98	145
(AZ, CA, HI, NV)	163	125	138	158	215	411
0 (AK, ID, OR, WA)	57	71	68	76	78	116
•			Crude rate (per			
II drug overdose deaths	0.53	0.51	0.61	1.32	2.57	5.67
-	0.33	0.01	0.01	1.02	2.31	J.0 <i>1</i>
Sex	0.00	0.50	0.74	4.00	0.70	0.40
ale	0.60	0.59	0.71	1.80	3.76	8.43
emale	0.47	0.44	0.51	0.86	1.41	3.00
Age group (years)						
5–24	0.29	0.25	0.36	1.03	2.11	4.42
5–34	0.78	0.78	0.97	2.81	6.10	13.38
5–44	0.93	0.86	0.99	2.45	4.90	11.40
5–54	1.13	1.12	1.26	2.23	3.72	8.25
5–64	0.69	0.68	0.83	1.22	2.19	4.78
5 and over	0.13	0.14	0.15	0.20	0.28	0.61
Race and Hispanic origin		_	_		_	
on-Hispanic white	0.75	0.73	0.84	1.78	3.41	7.07
on-Hispanic black	0.16	0.15	0.27	0.87	1.91	5.59
lispanic	0.12	0.09	0.18	0.40	0.79	2.43

Table 2. Numbers and crude and age-adjusted rates for drug overdose deaths involving fentanyl, by sex, age, race and Hispanic origin, and public health region: United States, 2011–2016—Con.

Characteristic	2011	2012	2013	2014	2015	2016					
Public health region ¹			Crude rate (per 1	00,000)							
1 (CT, ME, MA, NH, RI, VT)	0.53	0.53	1.07	5.54	11.65	19.79					
2 (NJ, NY, and NYC)	0.39	0.39	0.63	1.12	2.91	7.88					
3 (DE, DC, MD, PA, VA, WV)	0.70	0.64	0.94	1.95	3.88	11.87					
4 (AL, FL, GA, KY, MS, SC, TN)	0.67	0.66	0.71	1.48	2.79	5.70					
5 (IL, IN, MI, MN, OH, WI)	0.57	0.52	0.55	1.83	4.16	9.63					
6 (AR, LA, NM, OK, TX)	0.39	0.42	0.43	0.55	0.62	0.97					
7 (IA, KS, MO, NE)	0.61	0.81	0.91	1.02	1.66	3.78					
8 (CO, MT, ND, SD, UT, WY)	0.95	0.77	0.69	1.05	0.87	1.27					
9 (AZ, CA, HI, NV)	0.33	0.24	0.26	0.29	0.42	0.81					
10 (AK, ID, OR, WA)	0.43	0.53	0.48	0.58	0.56	0.89					
			Age-adjusted rate (per 100,000)								
All drug overdose deaths	0.53	0.52	0.61	1.34	2.64	5.89					
Sex											
Male	0.58	0.60	0.70	1.83	3.83	8.63					
Female	0.46	0.42	0.49	0.89	1.46	3.14					
Race and Hispanic origin											
Non-Hispanic white	0.74	0.72	0.83	1.86	3.68	7.74					
Non-Hispanic black	0.15	0.16	0.28	0.87	1.89	5.55					
Hispanic	0.12	0.09	0.18	0.43	0.78	2.47					
Public health region ¹											
1 (CT, ME, MA, NH, RI, VT)	0.53	0.53	1.07	5.54	11.65	19.79					
2 (NJ, NY, NYC)	0.39	0.39	0.63	1.12	2.91	7.88					
3 (DE, DC, MD, PA, VA, WV)	0.70	0.64	0.94	1.95	3.88	11.87					
4 (AL, FL, GA, KY, MS, SC, TN)	0.67	0.66	0.71	1.48	2.79	5.70					
5 (IL, IN, MI, MN, OH, WI)	0.57	0.52	0.55	1.83	4.16	9.63					
6 (AR, LA, NM, OK, TX)	0.39	0.42	0.43	0.55	0.62	0.97					
7 (IA, KS, MO, NE)	0.61	0.81	0.91	1.02	1.66	3.78					
8 (CO, MT, ND, SD, UT, WY)	0.95	0.77	0.69	1.05	0.87	1.27					
9 (AZ, CA, HI, NV)	0.33	0.24	0.26	0.29	0.42	0.81					
10 (AK, ID, OR, WA)	0.43	0.53	0.48	0.58	0.56	0.89					

Geographic regions defined by the U.S. Department of Health and Human Services (HHS), which are used for prevention, preparedness, and agency-wide coordination of HHS programs and policies. Region 1 includes Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont; Region 2 includes New Jersey, New York, and New York City; Region 3 includes Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia; Region 4 includes Alabama, Florida, Georgia, Kentucky, Mississippi, South Carolina, and Tennessee; Region 5 includes Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin; Region 6 includes Arkansas, Louisiana, New Mexico, Oklahoma, and Texas; Region 7 includes Iowa, Kansas, Missouri, and Nebraska; Region 8 includes Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming; Region 9 includes Arizona, California, Hawaii, and Nevada; Region 10 includes Alaska, Idaho, Oregon, and Washington.

NOTES: Drug overdose deaths are identified using *International Classification of Diseases, 10th Revision* underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to fentanyl. Caution should be used when comparing numbers across years. The reporting of at least one specific drug or drug class in the literal text, as identified by multiple cause-of-death codes T36–T50.8, improved from 75.0% of drug overdose deaths in 2011 to 85.4% in 2016.

Table 3. Trends in age-adjusted rates for drug overdose deaths involving fentanyl, by sex, age, race and Hispanic origin, and public health region: United States, 2011–2016

	Trend	1	Trend	2		
Characteristic	Years	Annual percent change	Years	Annual percent change	2011–2016 Average annual percent change	
All drug overdose deaths	2011–2013	8.5	2013–2016	113.3*	62.7*	
Sex						
Male	2011–2013	16.5	2013-2016	125.6*	73.2*	
- emale	2011-2016	58.9*			58.9*	
Age group (years)						
5–24	2011-2016	93.9*			93.9*	
5–34	2011-2016	100.0*			100.0*	
5–44	2011-2013	6.7	2013-2016	123.7*	66.4*	
5–54	2011-2016	60.3*			60.3*	
5–64	2011-2016	58.8*			58.8*	
5 and over	2011–2016	41.6*			41.6*	
Race and Hispanic origin						
Ion-Hispanic white	2011-2013	9.0	2013-2016	108.8*	61.0*	
lon-Hispanic black	2011-2016	140.6*			140.6*	
ispanic	2011–2016	118.3*			118.3*	
Public health region ¹						
(CT, ME, MA, NH, RI, VT)	2011-2016	113.9*			113.9*	
(NJ, NY, NYC)	2011-2016	110.9*			110.9*	
(DE, DC, MD, PA, VA, WV)	2011-2016	103.6*			103.6*	
(AL, FL, GA, KY, MS, SC, TN)	2011-2013	4.5	2013-2016	99.7*	54.1*	
(IL, IN, MI, MN, OH, WI)	2011-2016	102.2*			102.2*	
(AR, LA, NM, OK, TX)	2011-2016	20.8*			20.8*	
(IA, KS, MO, NE)	2011-2016	47.8*			47.8*	
(CO, MT, ND, SD, UT, WY)	2011-2016	7.1			7.1	
(AZ, CA, HI, NV)	2011-2014	-5.0	2014-2016	75.5	21.4	
(0 (AK, ID, OR, WA)	2011-2016	13.1*			13.1*	

^{*}Statistically significant increase at p value < 0.05. Trends in rates from 2011 through 2016 were evaluated using Joinpoint Regression Program (Version 4.6.0.0).

NOTES: Drug overdose deaths are identified using *International Classification of Diseases, 10th Revision* underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to fentanyl.

^{...} Category not applicable.

Geographic regions defined by the U.S. Department of Health and Human Services (HHS), which are used for prevention, preparedness, and agency-wide coordination of HHS programs and policies. Region 1 includes Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont; Region 2 includes New Jersey, New York, and New York City; Region 3 includes Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia; Region 4 includes Alabama, Florida, Georgia, Kentucky, Mississippi, South Carolina, and Tennessee; Region 5 includes Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin; Region 6 includes Arkansas, Louisiana, New Mexico, Oklahoma, and Texas; Region 7 includes Iowa, Kansas, Missouri, and Nebraska; Region 8 includes Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming; Region 9 includes Arizona, California, Hawaii, and Nevada; Region 10 includes Alaska, Idaho, Oregon, and Washington.

Technical Notes

Identification of fentanyl, fentanyl analogs, and misspellings on death certificate literal text fields

This report defines "drug overdoses involving fentanyl" as a drug overdose death involving fentanyl itself, including prescription fentanyl and illicitly manufactured fentanyl, as well as any fentanyl metabolites, precursors, and analogs identified in the death certificate text.

A search list for fentanyl was developed using the Scientific Working Group for the Analysis of Seized Drugs, which includes structurally confirmed reference materials generated by the United States Drug Enforcement Administration's special testing and research laboratory, and any monographs authored by the Forensic Drug Review and the Center for Forensic Science Research & Education (25). This list, combined with fentanyl analogs found in the U.S. Food and Drug Administration's (FDA) Substance Registration System (26) as of August 2017, is listed below. This search list was used to conduct an initial search of possible fentanyl terms mentioned in the literal text on death records from 2010 through 2016 using SAS Contextual Analysis software (18). If the term was found, a second analysis was conducted to identify misspellings of the term. The National Center for Health Statistics and FDA's Drugs Mentioned with Involvement (DMI) methodology was updated to include the new terms identified.

Fentanyl analogs identified in the literature, reports, and other sources are listed below:

3-METHYLFENTANYL*, 3-METHYLTHIOFENTANYL, 4-ANPP*, 4-CLORO-ISOBUTYLFENTANYL*, 4-FLUORO-ISOBUTYRYLFENTANYL*, 4-FLUORO-ISOBUTYRYLFENTANYL*, 4-MeO-BUTYRYLFENTANYL*, ABSTRAL, FENTANIL*, ACETYL-ALPHA-METHYLFENTANYL, ACETYLFENTANYL*, ACRYLFENTANYL*, ACRYLFENTANYL*, ACRYLOYLFENTANYL*, ACTIQ, ALFENTANIL*, ALPHA-METHYLTHIOFENTANYL, BENTANYL, BETA-HYDROXYF-S-METHYLFENTANYL, BETA-HYDROXYFENTANYL*, BUTYRYLFENTANYL*, CARFENTANIL*,

CROTONYLFENTANYL, CYCLOPROPYLFENTANYL, DESPROPIONYL-2-FLUOROFENTANYL, DESPROPIONYLFENTANYL*, DURAGESIC*, FENTANYL*, FENTORA, (2- or 3-) FURANYLFENTANYL*, IONSYS, ISOBUTYRYLFENTANYL*, LAZANDA, LOFENTANIL, META-FLUOROFENTANYL, METHOXYACETYLFENTANYL*, MIRFENTANYL, NORFENTANYL*, N-PHENETHYL-4-PIPERIDONE (NPP)*, OCFENTANIL, ONSOLIS, ORTHOFLUOROFENTANYL*, PARA-CHLOROFENTANYL,

PARA-CHLOROISOBUTYRFENTANYL, PARA-FLUOROBUTYRYL-FENTANYL*, PARA-FLUOROFENTANYL*, PARA-FLUOROISOBUTYRYLFENTANYL, PARA-METHODOXYBUTYRYLFENTANYL, REMIFENTANIL*, SUBLIMAZE, SUBSYS, SUFENTANIL*, TETRAHYDROFURANYLFENTANYL, THIOFENTANYL, VALERYLFENTANYL*

A comprehensive review for misspellings was conducted for terms with an asterisk because an exact pattern match of more than five records was found in the literal text fields for National Vital Statistics System—Mortality data for years 2010–2016.

The terms were grouped into broader fentanyl categories for reporting purposes. The term groupings are detailed in Table I according to the DMI methodology.

Methods for calculating and applying adjustment factor in trend analysis

The reporting of at least one specific drug involved in drug overdose deaths improved from 75.0% in 2011 to 85.4% in 2016 (2,22). Trend estimates may be impacted by the improvement in reporting that occurred during the study period. To assess the possible impact of the improved reporting of specific drugs in the years leading up to 2016, an adjustment factor was applied to each rate (i.e., by year, sex, age, race and ethnicity, and public health region) to calculate an adjusted rate. Drug specificity was determined for each year of the study as the percentage of drug overdose deaths with at least one International Classification of Diseases, 10th Revision (ICD-10) multiple cause-of-death code in the range of T36-T50.8. Drug specificity was calculated for each demographic and geographic subgroup in years 2011-2016 by taking the number of drug overdose deaths with codes T36-T50.8 divided by the number of drug overdose deaths in a given region and year (Table II). For example, in 2011, there were 41,340 drug overdose deaths, and among these, 30,993 of the deaths had a multiple-cause code of T36-T50.8, thus resulting in 75.0% drug specificity among drug overdose deaths in 2011. The same calculation applies to those in specific subgroups; in 2011, there were 2,941 drug overdose deaths among Hispanic persons, and 2,300 drug overdose deaths had a multiple-cause code of T36-T50.8, resulting in 78.2% drug specificity.

The adjustment factor (Table II) was calculated using the following assumptions for each year and subgroup: 1) from 2011 through 2015, the percentage of deaths with one or more drugs specified was equal to the percentage in 2016, and 2) the proportion of deaths involving fentanyl was the same for deaths that identified one or more specific drugs as for deaths that did not identify a specific drug. For example in 2011, there were 41,340 drug overdose deaths; the drug specificity was 75.0%, and 1,663 deaths involved fentanyl for an age-adjusted rate (AAR) of 0.53 per 100,000 standard population. To adjust for improved reporting:

- 1. Calculate the difference in percentage reporting in 2016 compared with 2011 (i.e., 85.4% 75.0% = 10.4%).
- 2. Multiply the difference in percentage reporting by the total number of drug overdose deaths in 2011 (i.e., 10.4% 41,340 = 4,299.36).
- Calculate the proportion of drug overdose deaths involving fentanyl among drug overdose deaths with one or more

- drugs specified in 2011 (i.e., $1,663 / [75.0\% \cdot 41,340] = 0.053636$).
- 4. Multiply the results from step 2 by the results from step 3 (i.e., $4,299.36 \cdot 0.053636 = 230.6$).
- 5. Calculate the adjustment factor by dividing the adjusted total drug overdose deaths involving fentanyl by the observed number of drug overdose deaths involving fentanyl (i.e., (1,663 + 230.6) / 1,663 = 1.14).
- 6. Calculate the adjusted AAR by multiplying the 2011 adjustment factor by the 2011 AAR rate (i.e., 0.53 * 1.14 = 0.60).

Table III shows the observed and adjusted age-adjusted death rates for each year by demographic and geographic group. The observed rates and number of drug overdose deaths involving any particular drug in any particular year should be considered the minimum number, as there may be additional deaths in which the drug was involved but not specified on the death certificate literal text. Observed and adjusted age-adjusted death rates resulted in similar findings after application of the adjustment factor (Table III).

Table I. Fentanyl groupings, as detailed in the Drugs Mentioned with Involvement methodology identified from National Vital Statistics System—Mortality literal text, 2010–2016

Principal variant ¹	Search terms
FENTANYL	ABSTRAL, ACETYL AND FENTANYL, ACTIQ, BENTANYL, DUEFENANYL, DURAGESIC, DURAHESIC, DURGESIC, F ENTANYL, FANTANIL, FANTANYL, FEBTANYL, FEDNTANYL, FENANYL, FENATANYL, FENATANYL, FENATANYL, FENATANYL, FENATANYL, FENATANYL, FENTANYL, FENTANIL, FENTANLY, FENTANUL, FENTANOL, FENTANOLY, FENTANOYL, FENTANTL, FENTANYL, RENTANYL, RENTANYL, SENTANYL, SUBSYS, TENTANYL
.BETAHYDROXYTHIOFENTANYL	B HYDROXYTHIOFENTANYL, BETA HYDROXYTHIOFENTANYL, BETAHYDROXYTHIOFENTANYL
3-METHYLFENTANYL	METHY FENTANYL, METHYFENTANYL, METHYL FENTANYL, METHYLFENTANYL
4-FLUOROBUTYRFENTANYL	F BF, FENTANYL ANALOGUES FURANYL PARAFLUROBUTYRYL AND DESPROPIONYL, FIBF, FLOROBUTYRYL FENTANYL, FLUOROBUTYL, FLUOROBUTYRYL FENTANYL, PEUOROBUTYRYL FENTANYL, PEUOROBUTYRYL FENTANYL, PEUOROBUTYRYL FENTANYL, PEUOROBUTYRYL FENTANYL, PARA FLUOROBUTYRYL FENTANYL, PARA FLUOROBUTYRYL FENTANYL, PARA FLUOROBUTYRYL FIBF, PARA FLUOROBUTYRYL PARA FLUOROBUTYRYL FENTANYL, PARA FLUOROBUTYRYL TENTANYL, PARA FLUOROBUTYRYLFENTANYL, PARA FLUOROBUTYRYL FENTANYL, PARA FLUOROBUTYRYL FENTANYL, PARA FLUOROBUTYRYL FENTANYL, PARAFLUOROBUTYRYL FENTANYL, PARAFLUOROBUTYRYL FENTANYL, PARAFLUOROBUTYRYL FENTANYL, PARAFLUOROBUTYRYL FENTANYL, PARAFLUOROBUTYRYL FENTANYL, PARAFLUOROBUTYRYL FENTANYL,
4-FLUOROISOBUTYRYLFENTANYL	DESPROPIONYL AND FLUORISOBUTYRYL FENTANYL, FLOUROISOBUTYRYL FENTANYL, FLUORISOBUTYRLFENTANYL, FLUORISOBUTYRLFENTANYL, FLUOROISOBUTYRYLFENTANYL, FLUOROISOBUTYRYL FENTANYL, FLUOROISOBUTYRYL FENTANYL, FLUOROISOBUTYRYL FENTANYL, FLUOROISOBUTYRYL FENTANYL, FLUOROISOBUTYRYL FENTANYL, FLUOROISOBUTYRYL FENTANYL, FLUROISOBUTYRYL FENTANYL, FLUROISOBUTYRYL FENTANYL, PHUOROISOBUTYRYL FENTANYL, PFLUOROISOBUTYRYL FENTANYL, PFLUOROISOBUTYRYL FENTANYL, PFLUOROISOBUTYRYL FENTANYL, PFLUOROISOBUTYRYL FENTANYL, PFLUOROISOBUTYRYL FENTANYL, PARA FLUOROISOBUTYRYL FENTANYL, PARAFLUOROISOBUTYRYL FENTANYL, PARAFLUOROISOBU
4-METHOXYBUTYRFENTANYL	METHOXY BUTYRYL FENTANYL
ACETYLFENTANYL	AACETYL FENTANYL, ACETANYL FENTANYL, ACETLY FENTANYL, ACETLYFENTANYL, ACETY FENTANYL, ACETY FENTANYL, ACETYFENTANYL, ACETYFENTANYL, ACETYFENTANYL, ACETYL FENTANYL, ACETYL FENTANYL, ACETYL FENTANYL, ACETYL FENTANYL, ACETYL FENTANYL N PHENETHYL PIPERIDYL ACETANILIDE, ACETYL FENTANYL PHENETHYL PIPERIDYL ACETANILIDE, ACETYL FENTANYL, ACETYL FENTANYL, ACETYL FENTANYL, ACETYL FENTANYL, ACETYL FENTANYL, ACETYL FENTANYL, ACETYLFENTAL, ACETYLFENTAL, ACETYLFENTAL, ACETYLFENTAL, ACETYLFENTANYL N PHENETHYL PIPERIDYL ACETANILIDE, ACETYLFENTANLY, ACETYLFENTANYL, ACETYLFENTANYL N PHENETHYL PIPERIDYL ACETANILIDE, ACETYLFENTANYL, ACETYLFENTANYL N PHENETHYL PIPERIDYL ACE, ACTEYL FENTANYL, FENTANYL AND ACETYL, N PHENETHY PIPER IDYL ACETANILIDE, N PHENETHYL PIPERIDYL ACETANILIDE, N PHENETHYL PIPERIDYL ACETANILIDE, N PHENETHYL PIPERIDYL ACETANILIDE, N PHENETHYL PIPERIDYL ACETANILIDE, PHENETHYL PIPERIDYL ACETANILIDE, TYL FENTANYL N PHENETHYL PIPERIDYL ACETANILIDE, PHENETHYL PIPERIDYL ACETANILIDE, TYL FENTANYL N PHENETHYL PIPERIDYL ACETANILIDE
ACRYLFENTANYL	ACRYIFENTANYL, ACRYL FENTANYL, ACRYLFENTANYL
ALFENTANIL	ALFENTANIL
BUTYRFENTANYL	BUTRYL FENTANYL, BUTYL FENTANYL, BUTYR FENTANYL, BUTYRFENTANYL, BUTYRYL FENTANYL, BUTYRYLFENTANYL
CARFENTANIL	CARENTANIL, CARENTANYL, CARFENTAIL, CARFENTANI, CARFENTANIL, CARFENTANILI, CARFENTANILI, CARFENTINAL, CARFENTINIL, CARFENTINIL, CARFENTINAL, CARFENTINIL, CARFENTINIL, CARFENTINIL, CARFENTINIL, CARFENTINIL, CARFENTINIL, CARFENTANIL

Table I. Fentanyl groupings, as detailed in the Drugs Mentioned with Involvement methodology identified from National Vital Statistics System—Mortality literal text, 2010–2016—Con.

Principal variant ¹	Search terms
DEPROPIONYLFENTANYL	ANILINE N PHENYTHYLPIPERIDINE, ANILINO N PHENETHYIPIPERIDINE, ANILINO N PHENETHYL PIPERIDINE, ANILINO N PHENETHYLPIPENDINE, ANILINO N PHENETHYLPIPERDINE, ANILINO N PHENETHYLPIPERIDINE, ANILINO N PHENETHYLPIPERIDINE, ANILIO N PHENETHYLPIPERIDINE, ANILO N PHENETHYLPIPERIDINE, ANPP, DEPROPIONLFENTANYL, DEPROPIONYL FENTANYL, DESPROPIONYL FENTANYL, DESPROPIONYL FENTANYL, DESPROPIONYL AND FLUORISOBUTYRYL FENTANYL, DESPROPIONYL ANILIO N PHENETHYLPIPERIDINE, DESPROPIONYL FENTANYL, DESPROPIONYL FENTANYL, DESPROPIONYL FENTANYL, DESPROPIONYL FENTANYL, FENTANYL, DESPROPIONYL FENTANYL, PENTANYL ANALOGUES FURANYL PARAFLUROBUTYRYL AND DESPROPIONYL, N PHENETHYL PIPERIDINE, N PHENYL PHENYLETHYL PIPERIDIN AMINE
FURANYLFENTANYL+	ACETYL FURANYL FENTANYL, DURANYLFENTANYL, FENTANYL ANALOGUES FURANYL PARAFLUROBUTYRYL AND DESPROPIONYL, FERANYL FENTANYL, FUNANYL FENTANYL, FURANULFENTANYL, FURANY FENTANUL, FURANY FENTANYL, FURANYFENTANYL, FURANYIFENTANYL, FURANYL FENTANYL, FURANYLFANTANYL, FURANYLFENTANTL, FURANYLFENTANYL, FURANYLFENTANYLM, FURANYLTENTANYAL, FURANYLTENTANYL, FURAYLFENTANY, FURAYLFENTANYL, FURFANYLFENTANYL, FURNYL FENTAYL, FURTANYL FENTANYL, FURYL FENTANYL, TURANYL FENTANYL
ISOBUTYRFENTANYL	ISOBUTYRYLFENTANYL
METHOXYACETYLFENTANYL	METHOXYACETYL FENTANYL
METHYLFENTANYL+	CIS METHYLFENTANYL
NORALFENTANIL	NORALFENTANIL
NORFENTANYL	NORENTANYL, NORFENTANLY, NORFENTANYL, NORFETANYL, NORPHENTANYL
ORTHO-FLUOROFENTANYL	ORTHO FLUOROFENTANYL
P-FLUOROFENTANYL	FLUORA FENTANYL, FLUOROFENTANYL, FLURODENTANYL, FLUROFENTANYL, FLUROROFENTANYL, PARAFLUROFENTANYL, PARAFLUORO FENTANYL
REMIFENTANIL	REMIFENTANIL, REMIFENTANYL
SUFENTANIL	SUFENTANIL
AMBIGUOUS (FENTANYL or TEGAFUR)	FENTALY, FENTAYL, FENTYAL, FENTYL
AMBIGUOUS (NORALFENTANIL or NORFENTANYL)	NOAFENTANYL

¹The overarching label assigned to a drug, a drug class, or exposure not otherwise specified in the Drugs Mentioned with Involvement methodology. For example, terms such as "COCAINE," "COCAINE CRACK," "COCAINE HYDROCHLORIDE," and "COCAINETOXICITY" are all mapped to the principal variant "COCAINE." In the case of drug overdose deaths involving fentanyl, all of the principal variants in this table were used to calculate the numbers and rates presented in this report.

Table II. Percent of drug overdose deaths with drugs specified, by sex, age, race and Hispanic origin, and public health region: United States, 2011–2016

			Per	cent					Adjustm	ent factor		
Characteristic	2011	2012	2013	2014	2015	2016	2011	2012	2013	2014	2015	2016
All drug overdose deaths	75.0	76.0	77.9	80.7	83.1	85.4	1.14	1.12	1.10	1.06	1.03	1.00
Sex												
Male	84.5	86.2	88.1	90.4	91.8	93.4	1.12	1.11	1.08	1.04	1.02	1.00
Female	77.5	78.4	79.8	82.5	86.1	88.5	1.16	1.15	1.12	1.08	1.03	1.00
Age group (years)												
15–24	77.9	78.7	81.9	83.2	84.8	87.2	1.12	1.11	1.06	1.05	1.03	1.00
25–34	75.1	76.4	79.2	82.0	84.1	86.0	1.15	1.12	1.09	1.05	1.02	1.00
35-44	73.8	75.4	76.5	80.2	82.8	85.5	1.16	1.13	1.12	1.07	1.03	1.00
45-54	74.2	74.8	77.0	79.7	81.7	84.8	1.14	1.13	1.10	1.06	1.04	1.00
55-64	74.4	75.7	77.0	79.3	82.5	84.8	1.14	1.12	1.10	1.07	1.03	1.00
65 and over	79.8	79.2	80.0	81.7	84.7	84.9	1.06	1.07	1.06	1.04	1.00	1.00
Race and Hispanic origin												
Non-Hispanic white	73.9	74.7	76.5	79.8	82.4	84.6	1.13	1.10	1.06	1.04	1.03	1.00
Non-Hispanic black	80.7	82.6	84.5	83.8	85.6	88.4	1.14	1.13	1.10	1.06	1.03	1.00
Hispanic	78.2	80.4	83.1	84.7	85.3	88.1	1.09	1.07	1.05	1.05	1.03	1.00
Public health region ¹												
1 (CT, ME, MA, NH, RI, VT)	90.6	89.0	97.4	98.9	98.8	98.9	1.09	1.11	1.01	1.00	1.00	1.00
2 (NJ, NY, NYC)	82.5	83.5	85.2	86.7	86.8	90.2	1.09	1.08	1.06	1.04	1.04	1.00
3 (DE, DC, MD, PA, VA, WV)	70.8	71.2	74.1	74.3	73.6	76.0	1.07	1.07	1.03	1.02	1.03	1.00
4 (AL, FL, GA, KY, MS, SC, TN)	70.4	71.7	72.4	78.4	82.0	83.8	1.19	1.17	1.16	1.07	1.02	1.00
5 (IL, IN, MI, MN, OH, WI)	73.5	74.9	76.9	79.9	83.9	89.3	1.21	1.19	1.16	1.12	1.06	1.00
6 (AR, LA, NM, OK, TX)	69.9	74.8	76.0	76.9	79.9	81.8	1.17	1.09	1.08	1.06	1.02	1.00
7 (IA, KS, MO, NE)	78.2	78.4	77.9	81.5	83.3	84.7	1.08	1.08	1.09	1.04	1.02	1.00
8 (CO, MT, ND, SD, UT, WY)	78.0	78.1	82.5	85.4	84.9	85.3	1.09	1.09	1.03	1.00	1.00	1.00
9 (AZ, CA, HI, NV)	75.8	74.3	75.3	77.7	81.2	83.2	1.10	1.12	1.11	1.07	1.02	1.00
10 (AK, ID, OR, WA)	89.8	90.3	90.0	91.0	92.1	92.1	1.03	1.02	1.02	1.01	1.00	1.00

'Geographic regions defined by the U.S. Department of Health and Human Services (HHS), which are used for prevention, preparedness, and agency-wide coordination of HHS programs and policies. Region 1 includes Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont; Region 2 includes New Jersey, New York, and New York City; Region 3 includes Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia; Region 4 includes Alabama, Florida, Georgia, Kentucky, Mississippi, South Carolina, and Tennessee; Region 5 includes Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin; Region 6 includes Arkansas, Louisiana, New Mexico, Oklahoma, and Texas; Region 7 includes lowa, Kansas, Missouri, and Nevada; and Region 10 includes Alaska, Idaho, Oregon, and Washington

NOTE: Drug specificity is calculated by taking the number of drug overdose deaths (International Classification of Diseases, 10th Revision [ICD-10] underlying cause-of-death codes X40-X44, X60-X64, X85, and Y10-Y14) with ICD-10 multiple cause-of-death codes T30-T50.8, divided by the number of drug overdose deaths in a given region and year.

Table III. Rates of drug overdose deaths involving fentanyl, observed and adjusted for improved specificity, by sex, age, race and Hispanic origin, and public health region: United States, 2011–2016

			Observed	death rate			Number of			Adjusted	death rate			Number of
Characteristic	2011	2012	2013	2014	2015	2016	joinpoints in final model (time point)	2011	2012	2013	2014	2015	2016	joinpoints ir final model (time point)
All drug overdose deaths	0.53	0.52	0.61	1.34	2.64	5.89	1 (2013)*	0.60	0.59	0.67	1.42	2.71	5.89	1 (2013)*
Sex														
Male	0.58	0.60	0.70	1.83	3.83	8.63	1 (2013)*	0.65	0.66	0.75	1.91	3.92	8.63	1 (2013)*
Female	0.46	0.42	0.49	0.89	1.46	3.14	` - (*)	0.53	0.49	0.54	0.96	1.51	3.14	· - (*)
Age group (years)														
15–24	0.29	0.25	0.36	1.03	2.11	4.42	- (*)	0.33	0.28	0.39	1.08	2.17	4.42	- (*)
25-34	0.78	0.78	0.97	2.81	6.10	13.38	- (*´)	0.89	0.88	1.05	2.95	6.23	13.38	- (*)
35-44	0.93	0.86	0.99	2.45	4.90	11.40	1 (2013)*	1.08	0.98	1.10	2.61	5.06	11.40	1 (2013)*
45-54	1.13	1.12	1.26	2.23	3.72	8.25	- (*)	1.29	1.28	1.39	2.38	3.86	8.25	- (*)
55-64	0.69	0.68	0.83	1.22	2.19	4.78	- (*)	0.79	0.76	0.91	1.30	2.25	4.78	- (*)
65 and over	0.13	0.14	0.15	0.20	0.28	0.61	- (*)	0.14	0.15	0.16	0.20	0.28	0.61	- (*)
Race and Hispanic origin														
Non-Hispanic white	0.74	0.72	0.83	1.86	3.68	7.74	1 (2013)*	0.85	0.81	0.92	1.97	3.78	7.74	1 (2013)*
Non-Hispanic black	0.15	0.16	0.28	0.87	1.89	5.55	· - (*)	0.17	0.17	0.29	0.92	1.95	5.55	- (*)
Hispanic	0.12	0.09	0.18	0.43	0.78	2.47	- (*)	0.13	0.10	0.19	0.44	0.80	2.47	- (*)
Public health region ¹														
1 (CT, ME, MA, NH, RI, VT)	0.53	0.53	1.07	5.54	11.65	19.79	- (*)	0.58	0.58	1.09	5.53	11.66	19.79	- (*)
2 (NJ, NY, NYC)	0.39	0.39	0.63	1.12	2.91	7.88	- (*)	0.43	0.42	0.67	1.16	3.02	7.88	- (*)
3 (DE, DC, MD, PA, VA, WV)	0.70	0.64	0.94	1.95	3.88	11.87	- (*)	0.76	0.68	0.96	1.99	4.00	11.87	- (*)
4 (AL, FL, GA, KY, MS, SC, TN)	0.67	0.66	0.71	1.48	2.79	5.70	1 (2013)*	0.79	0.77	0.82	1.58	2.85	5.70	1 (2013)*
5 (IL, IN, MI, MN, OH, WI)	0.57	0.52	0.55	1.83	4.16	9.63	- (*)	0.70	0.62	0.64	2.05	4.43	9.63	- (*)
6 (AR, LA, NM, OK, TX)	0.39	0.42	0.43	0.55	0.62	0.97	- (*)	0.46	0.46	0.46	0.59	0.64	0.97	- (*)
7 (IA, KS, MO, NE)	0.61	0.81	0.91	1.02	1.66	3.78	- (*)	0.66	0.87	0.98	1.06	1.69	3.78	- (*)
8 (CO, MT, ND, SD, UT, WY)	0.95	0.77	0.69	1.05	0.87	1.27	-	1.04	0.85	0.72	1.05	0.87	1.27	_
9 (AZ, CA, HI, NV)	0.33	0.24	0.26	0.29	0.42	0.81	1 (2014)	0.37	0.26	0.29	0.31	0.43	0.81	1 (2014)
10 (AK, ID, OR, WA)	0.43	0.53	0.48	0.58	0.56	0.89	- (*)	0.45	0.54	0.49	0.58	0.56	0.89	- (*)

^{*}Statistically significant increases at p value < 0.05. Trends in rates from 2011 through 2016 were evaluated using Joinpoint Regression Program (Version 4.6.0.0).

NOTES: Drug overdose deaths are identified using International Classification of Diseases, 10th Revision underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to fentanyl. Death rates are age adjusted.

⁻ Quantity zero.

Geographic regions defined by the U.S. Department of Health and Human Services (HHS), which are used for prevention, preparedness, and agency-wide coordination of HHS programs and policies. Region 1 includes Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont; Region 2 includes New Jersey, New York, and New York City; Region 3 includes Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia; Region 4 includes Alabama, Florida, Georgia, Kentucky, Mississippi, South Carolina, and Tennessee; Region 5 includes Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin; Region 6 includes Arkansas, Louisiana, New Mexico, Oklahoma, and Texas; Region 7 includes Iowa, Kansas, Missouri, and Nebraska; Region 8 includes Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming; Region 9 includes Arizona, California, Hawaii, and Nevada; and Region 10 includes Alaska, Idaho, Oregon, and Washington.

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

Centers for Disease Control and Prevention National Center for Health Statistics 3311 Toledo Road, Room 4551, MS P08 Hyattsville, MD 20782–2064

OFFICIAL BUSINESS PENALTY FOR PRIVATE USE, \$300

For more NCHS NVSRs, visit: https://www.cdc.gov/nchs/products/nvsr.htm.



National Vital Statistics Reports, Vol. 68, No. 3, March 21, 2019

Contents

Acknowledgments

FIRST CLASS MAIL

POSTAGE & FEES PAID CDC/NCHS

PERMIT NO. G-284

The authors would like to acknowledge the contributions of Lauren Rossen, Katherine E. Irimata, and Donald Malec of the National Center for Health Statistics, for their guidance on the trends analysis; and Bruce Goldberger at the University of Florida College of Medicine and Barry Logan at NMS Labs, for their expert toxicological input on fentanyl terms, analogs, derivatives, and other forms.

Suggested citation

Spencer MR, Warner M, Bastian BA, Trinidad JP, Hedegaard H. Drug overdose deaths involving fentanyl, 2011–2016. National Vital Statistics Reports; vol 68 no 3. Hyattsville, MD: National Center for Health Statistics. 2019.

Copyright information

All material appearing in this report is in the public domain and may be reproduced or copied without permission; citation as to source, however, is appreciated.

National Center for Health Statistics

Jennifer H. Madans, Ph.D., *Acting Director*Amy M. Branum, Ph.D., *Acting Associate Director for Science*

Office of Analysis and Epidemiology

Irma E. Arispe, Ph.D., *Director*Irma E. Arispe, Ph.D., *Acting Associate Director for Science*

Division of Vital Statistics

Steven Schwartz, Ph.D., *Director* Hanyu Ni, Ph.D., M.P.H., *Associate Director for Science*